UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/827,371	04/06/2001	David Hung	05284.00085	3897

38732 7590 08/29/2006

CYTYC CORPORATION
250 CAMPUS DRIVE
MARLBOROUGH, MA 01752

EXAMINER	
FLOOD, MICHELE C	

ART UNIT	PAPER NUMBER
1655	

DATE MAILED: 08/29/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/827,371	HUNG, DAVID	
	Examiner	Art Unit	
	Michele Flood	1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 June 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,6 and 22-27* is/are pending in the application.

4a) Of the above claim(s) *24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,6,22,23 and 25-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of the species mannitol in the reply filed on June 13, 2006 is acknowledged. Applicant states that the elected species is readable on Claims 1, 6 and 22. However, this is not persuasive since the subject matter of Claim 22 is directed to 'The method of claim 1 wherein the agent is a nonabsorbable biocompatible solution'. The Office deems that the elected species is readable on Claims 1, 6 and 23.

The originally elected species was not found; therefore the claim was examined on the merits until the next species of the claim was found.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 6, 7, and 22-27 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for preparing for intraductal retrieval of fluid, cells and/or other material from a breast duct of a patient comprising administering intraductally to the patient an effective amount of mannitol that

increases the ductal fluid collection from a breast duct of a patient, does not reasonably provide enablement for the claim-designated method comprising the intraductal administration of any and all amounts of any and all of the agents recited in the Markush group of Claim 1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims, as broadly claimed by Applicant.

The claims are drawn to a method for increasing retrievable intraductal retrievable fluid, cells and/or other material from a breast duct of a patient comprising administering intraductally to the patient an agent that increases the secretion of ductal fluid into a breast duct, wherein the agent is selected from the group consisting of a hypotonic solution, a buffered solution, a nonabsorbable biocompatible solution, a protein, a colloid, a sugar, a polymer, mannitol, sorbitol, glucose, glycerol, sucrose, raffinose, fructose, lactulose, polyethyleneglycol (PEG), maltodextrin, dextran, dextran 70, hydroxyethyl starch, fluid gelatin, a synthetic colloid, an antibody, a binding protein, albumin, a hormone, a natural herb, an extract from a natural herb, silymarin, a surfactant, a growth factor, oxytocin, prolactin, an organic molecule, a muscle relaxant, and a ductal orifice dilator. Applicant further claims the method as in claim 1, wherein the agent is a nonabsorbable biocompatible solution.

The factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) (a) the breadth of the claims; (b) the nature of the invention; (c) the state of the prior art; (d) the level of one of ordinary skill in the art; (f) the amount of direction

provided by the inventor; (g) the existence of working examples; and (h) the quantity of experimentation added to make or use the invention based on the content of the disclosure. While all of these factors are considered, a sufficient number are discussed below so as to create a *prima facie* case.

While Applicant has reasonably demonstrated a method for increasing retrievable intraductal fluid, cells and/or other material from a breast duct of a patient comprising the intraductal administration of an effective amount of mannitol that increases the ductal fluid into a breast duct, Applicant has not demonstrated a method for increasing retrievable intraductal fluid, cells and/or other material from a breast duct of a patient comprising the intraductal administration of any and all of the agents recited in the Markush group of Claim 1 in any and all amounts to provide the claim-designated functional effect to increase secretion of ductal fluid into a breast duct of a patient. For instance, on page 14 of the specification, line 20 to page 16, Applicant exemplifies a method of intraductally administering an effective amount of mannitol in water to the breast of a rabbit to provide the claim-designated functional effect to increase ductal fluid collection. However, Applicant has not demonstrated a method for increasing retrievable intraductable fluid, cells and/or other material from a breast duct of a patient comprising the intraductal administration of any and any of the claim-designated agents in any and all amounts, wherein the intraductal administration of any of the claim-designated agents increase secretion of ductal fluid into the breast of a patient, as broadly claimed by Applicant.

While it may be possible that particular agents recited in the Markush group of Claim 1 could increase the secretion of ductal fluid into a breast duct of a patient such as hormones, it is highly unlikely that any and all of the claim-designated agents could increase secretion of ductal fluid into a breast duct. The Office notes that on page 5, lines 20-24, Applicant expressly states, "The invention is the discovery that by first artificially increasing the fluid volume or fluid reservoir in a breast one can collect sufficient ductal fluid for analysis of the duct and breast." On page 8 of the specification, lines 3-24, it appears that Applicant discloses that the intraductal administration of some of the claim-designated agents may not indeed increase secretion of ductal fluid but rather increase or at least maintain the amount of collectable fluid already present in the lumen of the breast duct. It should be noted that the state of the art at the time the invention was made did not recognize that all of the instantly claimed agents could increase the secretion of ductal fluid into to the breast of a duct. For instance, Nikodem et al. (W, Birth, 1993, 20:61-64. *Do cabbage leaves prevent breast engorgement?*) teach that cabbage leaf extract discourages the secretion of fluid into the breast duct of a patient. There is no guidance in the specification, other than the administration of effective amounts of mannitol to increase ductal fluid collection from a breast duct. Moreover, the instant application does not provide a working example providing data which shows that the composition of the instant claims would indeed increase secretion of fluid into a breast duct of a patient comprising any of the claim-designated ingredients. Thus, Applicant has not demonstrated that any and all of the claim-designated agents have the claimed functional effect of increasing secretion of ductal

fluid into a breast duct of a patient when intraductally administered to provide the instantly claimed method of as broadly claimed, other than the aforementioned and demonstrated disease condition. Accordingly, it would take undue experimentation without a reasonable expectation of success for one skill in the art to make and/or use the method, as broadly claimed by Applicant.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1,6, 22, 23 and 25-27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites the limitation "the secretion of ductal fluid" in lines 3-4. There is insufficient antecedent basis for this limitation in the claim.

All other cited claims depend directly or indirectly from rejected claims and are, therefore, also, rejected under U.S.C. 112, second paragraph for the reasons set forth above.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 and 22 are rejected under 35 U.S.C. 102(b) as being anticipated by Love et al. (A*).

Applicant claims a method for increasing retrievable intraductal retrievable fluid, cells and/or other material from a breast duct of a patient comprising administering intraductally to the patient an agent that increases the secretion of ductal fluid into a breast duct, wherein the agent is selected from the group consisting of a hypotonic solution, a buffered solution, a nonabsorbable biocompatible solution, a protein, a colloid, a sugar, a polymer, mannitol, sorbitol, glucose, glycerol, sucrose, raffinose, fructose, lactulose, polyethyleneglycol (PEG), maltodextrin, dextran, dextran 70, hydroxyethyl starch, fluid gelatin, a synthetic colloid, an antibody, a binding protein, albumin, a hormone, a natural herb, an extract from a natural herb, silymarin, a surfactant, a growth factor, oxytocin, prolactin, an organic molecule, a muscle relaxant, and a ductal orifice dilator. Applicant further claims the method as in claim 1, wherein the agent is a nonabsorbable biocompatible solution.

Love teaches the intraductal administration of physiological saline to a breast duct for the retrieval of fluid, cells and/or other material from a breast of a patient. In Column 6, lines 55-67, Love discloses that "The volume of fluid introduced into the ductal network D_2 will be sufficiently large so that substantially the entire volume of the ductal network may be filled with the washing fluid and excess fluid will flow from the network as it is displaced by additional fluid input . . . The remaining fluid will continue to be introduced and will thus flush the cellular and other marker materials from the ductal network into the opening . . ." After collection of the washing fluid comprising the

retrievable fluid obtained from the breast duct through a double lumen catheter, Love teaches analyzing the fluid to identify a marker of a breast condition (see Column 5, lines 38-44). Given the claims the broadest interpretation of the term "an organic molecule", the Examiner regards the physiological saline washing fluid taught by Love as an "organic molecule".

The reference anticipates the claimed subject matter.

Claims 1, 6, 22, 25 and 27 are rejected under 35 U.S.C. 102(b) as being anticipated by Martyn et al. (V), as evidenced by the teachings of Kartinos et al. (B*) and Mullins (C*).

Martyn teaches a method increasing retrievable intraductal fluid, cells and/or other material from a breast duct of a patient comprising administering intraductally to the patient prolactin as either an emulsion or an aqueous solution, made by dissolving prolactin in NaOH and diluting with phosphate buffered saline containing Blue Dextran (a nonabsorbable biocompatible solution, as evidenced by the teachings of Kartinos and Mullins). The emulsion was prepared by sonicating an aqueous solution phase consisting of phosphate buffer saline containing bovine serum albumin and Blue Dextran with safflower oil (see page 323. Column 2, under *"Mammary intraductal injections"*. In Table 1, Martyn shows that glycerolipid synthesis in the mammary gland was significantly enhanced in the presence of insulin, corticosterone and prolactin; addition of prolactin stimulated acetyl-CoA carboxylase activity; prolactin together with insulin and corticosterone stimulated activity of fatty acid synthetase; glucose-6-

phosphate dehydrogenase was enhanced with prolactin injection. On page 326, Column 1, lines 9-27, Martyn teaches that intraductal injection of prolactin, or prolactin plus progesterone, had more secretion than did untreated emulsion treated or progesterone-treated glands within the same patient.

The reference anticipates the claimed subject matter.

Claims 1, 6, 22, 25 and 27 are rejected under 35 U.S.C. 102(b) as being anticipated by Falconer et al. (U), as evidenced by the teachings of Kartinos et al. (B) and Mullins (C).

On page 182, Column 2, lines 6-15, Falconer teaches a method for increasing intraductal retrieval of fluid, cells and/or other material from a breast duct of a patient comprising administering intraductally to the patient prolactin (a growth hormone), ouabain or both dissolved in a solution of [Na+], [K+] and [Cl-] containing Dextran Blue 2000 (a nonabsorbable biocompatible solution, as evidenced by the teachings of Kartinos and Mullins). Falconer further teaches removing and sampling alveolar tissue associated with the injected duct systems for water content determinations and Na+, K+ and Cl- and [14C]-lactose analysis, on page 184, Column 2, lines 29-33. In Table 1, Falconer shows that increasing the amounts of prolactin increased the water content of wet tissue in the treated mammary gland tissue. On page 184, Column 1, lines 13-19 bridging Column 2, lines 1-6, Falconer teaches *in vivo* intraductal injection of prolactin to a patient showed an increase [K+] of 10 mmol/kg wet tissue (see Table 3); whereas, *in vivo* intraductal administration of prolactin and ouabain an increase [Na+]. On page

182, Column 2, lines 14-19, Falconer teaches an increased extracellular water content of the ouabain-treated glands (*see* Table 3). Table 3 also shows an increased extracellular water content of the prolactin-treated glands, as well.

The reference anticipates the claimed subject matter.

* Applicant is advised that the cited U.S. patents and patent application publications are available for download via the Office's PAIR. As an alternate source, all U.S. patents and patent application publications are available on the USPTO web site (www.uspto.gov), from the Office of Public Records and from commercial sources. Should you receive inquiries about the use of the Office's PAIR system, applicants may be referred to the Electronic Business Center (EBC) at http://www.uspto.gov/ebc/index.html or 1-866-217-9197.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michele Flood whose telephone number is 571-272-0964. The examiner can normally be reached on 7:00 am - 3:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Terry McKelvey can be reached on 571-272-0775. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

MICHELE FLOOD
PRIMARY EXAMINER

Michele Flood
Primary Examiner
Art Unit 1655

MCF
August 21, 2006